IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

PAR PHARMACEUTICAL, INC., PAR STERILE PRODUCTS, LLC, and ENDO PAR INNOVATION COMPANY, LLC, Plaintiffs, v. EAGLE PHARMACEUTICALS INC., Defendant.	)	C.A. No. 18-823-CFC
PAR PHARMACEUTICAL, INC., PAR STERILE PRODUCTS, LLC, and ENDO PAR INNOVATION COMPANY, LLC, Plaintiffs, v. AMNEAL PHARMACEUTICALS OF NEW YORK, LLC, et al., Defendant.	)	C.A. No. 18-2032-CFC

DEFENDANTS' PROPOSED CONCLUSIONS OF LAW
ON INVALIDITY AND UNENFORCEABILITY

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I. INTRODUCTION

Stable vasopressin formulations have been used to treat hypotension for a century, since before the FDA regulated drugs. (FF¶26.) Through a controversial program aimed at bringing pre-FDA drugs into the system, Par filed a "paper NDA" for its decades-old formulation, relying only on literature. (FF¶¶35.) The result was the 2014 approval of Original Vasostrict, which was used for several years without safety or stability concerns. (FF¶¶37, 77.) Under the FDA program, Par secured a temporary monopoly until generics could secure approved ANDAs on the old formulation. To that end, Eagle seeks approval of a generic version of Original Vasostrict.

After approval, however, Par tweaked Vasostrict's formulation by raising the manufacturing pH—allegedly to improve stability—and replaced Original Vasostrict with Reformulated Vasostrict in the market. (FF¶41.) Par's '209 and '785 patents ("the Asserted Patents") are directed to Reformulated Vasostrict, require pH 3.7–3.9, and admittedly do not cover Original Vasostrict. (FF¶64.) Yet in this case, Par is using them to delay generic versions of ***Original Vasostrict***. (*See* FF¶133.)

That tension exacerbates already insurmountable invalidity problems. The asserted claims differ from prior art Original Vasostrict only by their abutting pH ranges: 3.4–3.6 (3.35–3.64 with rounding) for Original Vasostrict, and 3.7–3.9 (3.65–3.94 with rounding) for the asserted claims. (FF¶314.) A presumption of

obviousness thus exists, shifting the burden of production to Par to show criticality of the claimed pH, or that the prior art taught away from it. Par cannot meet it—its expert conceded one would not even be able to detect a stability difference between formulations within (3.65) and outside (3.64) the claimed pH range. (FF¶158.)

Moreover, to capture Eagle's ANDA product, Par argues the claims cover formulations manufactured within the prior art pH range 3.4–3.6, but that ***drift*** into the claimed range for as little as five minutes. (FF¶61.) There is no criticality or teaching away because all experts and inventors agree that no study, document or other evidence even addresses such a formulation. (FF¶¶168–71, 182, 194–95, 214.) And expectedly, Reformulated Vasostrict has provided ***no*** material stability benefit, much less a critical one. Its shelf life and impurities specifications are the same as Original Vasostrict's. (FF¶¶89–90, 175, 185, 187.)

This begs the question of how Par secured the Asserted Patents over Original Vasostrict. Clear and convincing evidence shows that only happened as a result of three unmistakably false declarations by inventor Kannan, submitted by prosecuting attorney Kenesky, during Par's prosecution of related patents. The false declarations were submitted in direct response to pointed questions from the Examiner, and Kannan knew at the time they would be used "to overcome the Patent Examiner's concern about [Original Vasostrict's label] being prior art that would invalidate the patent," and to represent submitted pH study data as "truly significant" rather than

the result of it being obtained in "two separate experiments." (FF¶¶269,302.) As will be discussed, false declarations are material as a matter of law, and the single most reasonable inference is that they were intended to deceive the PTO.

Thus, clear and convincing evidence establishes the obviousness of the asserted claims, and that they were acquired through inequitable conduct.

II. THE ASSERTED CLAIMS ARE OBVIOUS OVER ORIGINAL VASOSTRICT

A patent "may not be obtained … if the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious before the effective filing date of the claimed invention to a person having ordinary skill in the art [("POSA")] to which the claimed invention pertains." 35 U.S.C. §103 (2011). Per the Supreme Court, §103 ensures that "the results of ordinary innovation are not the subject of exclusive rights under the patent laws," and that a patentee is not "withdraw[ing] what already is known into the field of its monopoly and diminish[ing] the resources available to skillful men," *KSR Intern. Co. v. Teleflex Inc.*, 550 U.S. 398, 415, 427 (2007).

Generally, "[a] showing of obviousness requires a motivation or suggestion to combine or modify prior art references, coupled with a reasonable expectation of success" to arrive at the claimed invention. *Boehringer Ingelheim Vetmedica, Inc. v. Schering-Plough Corp.*, 320 F.3d 1339, 1354 (Fed. Cir. 2003). The Court then considers evidence of "secondary considerations" of nonobviousness. *See KSR*, 550

U.S. at 399. But in certain situations, a "presumption of obviousness" applies and the burden of production shifts to the patentee. This is one such situation.

A. The Presumption Of Obviousness Applies Here

The presumption of obviousness applies here because the only difference between the asserted claims and Original Vasostrict[1] is their abutting pH ranges. The Federal Circuit has "held that a *prima facie* case[2] of obviousness exists when the claimed range and the prior art range do not overlap but are close enough such that one skilled in the art would have expected them to have the same properties." *In re Peterson*, 315 F.3d 1325, 1329 (Fed. Cir. 2003). That is because "[w]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Applied Materials, Inc.*, 692 F.3d 1289, 1295 (Fed. Cir. 2012). For example, in *In re Woodruff*, claims requiring "*more than 5%* to about 25%" CO_2 were presumed obvious where the prior art taught an abutting range of "about 1–*5%*." 919 F.2d 1575, 1578 (Fed. Cir. 1990).

Here, Original Vasostrict satisfied every clinical, formulation, and impurity limitation of the asserted claims, with an abutting pH, triggering the presumption:

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[1] Original Vasostrict was FDA-approved, sold with its label, and publicly used to treat hypotension for over two years before the Asserted Patents' priority date. (FF¶¶37, 77.)

[2] Courts use "*prima facie* case" and "presumption of obviousness" interchangeably. *See Genentech, Inc. v. Hospira, Inc.*, 946 F.3d 1333, 1341 (Fed. Cir. 2020).

Clinical limitations ('209 patent): The asserted claims recite "[a] method of increasing blood pressure in a human," where "the human is hypotensive," by administering "from about 0.01 units of vasopressin … per minute to about 0.1 units of vasopressin … per minute." (FF¶58.) The label accompanying Original Vasostrict instructed its use to treat hypotension (*i.e.*, to increase blood pressure) at the exact dosages recited—"anywhere between 0.01 units per minute to a ceiling of 0.1 units per minute." (FF¶85.) Par did not dispute this.

Formulation limitation (both Asserted Patents): The Asserted Patents recite the "dosage form comprises from about 0.01 mg/mL to about 0.07 mg/mL of vasopressin …." (FF¶¶58–59.) Original Vasostrict comprised 20 units/mL—0.0377 mg/mL—within the claimed range. (FF¶87.) Par did not dispute this.

Impurities limitations (both Asserted Patents): The Asserted Patents recite the "dosage form further comprises impurities that are present in an amount of 0.9%–1.7%, wherein the impurities have from about 85% to about 100% sequence homology to SEQ ID NO. 1," *i.e.*, vasopressin. (FF¶¶58–59.) The asserted dependent claims recite particular impurity ranges. *Id*. Representative lots of Original Vasostrict, including registration Lot 310571, and commercial Lots 788435 and 788436 sold before the Asserted Patents' priority date, met these limitations:

Claims		Limitation	Lot 788435 (12 Months)	Lot 788436 (Initial)	Lot 310571	
'209	'785				Initial	3 Mos.
1	1	0.9–1.7% homologous	0.9% (homologous) 1.7% (total)[3]	0.7% (homologous) 1.6% (total)	0.8%	1.8%[4]
2		0.1–0.3% Gly9	0.3%	0.1%	0.1%	0.5%
4	5	0.2–0.4% Glu4	0.3%		0.1%	0.6%
5		0.3–0.6% Acetyl	0.2%	0.4%	0.25%	0.26%
6		0.1% D-Asn	0.1%			
7	8	0.1–0.3% Gly9 0.2–0.4% Glu4	0.3% 0.3%		0.1% 0.1%	0.5% 0.6%
8		0.1% Asp5 0.3–0.6% Acetyl 0.1% D-Asn	0.0% 0.2% 0.1%			

(DTX-360.25–26; DTX-45.7; DTX-1314.1; FF¶¶108–14, 117–21, 127–31.)

That the impurity (and pH, discussed below) measurements were reported in Par's internal documents, (*see* Tr. 426:13–27:6), is irrelevant. "If a product that is offered for sale inherently possesses each of the limitations of the claims, then the invention is on sale, whether or not the parties to the transaction recognize that the product possesses the claimed characteristics." *Abbott Lab'ys v. Geneva Pharms.*,

[3] At 12 months, Lot 788435 had 0.9% impurities identified as homologous to SEQ ID NO. 1 (vasopressin), and another 0.8% unidentified impurities with unknown homology. (FF¶¶108–09.) But if both the homologous and total impurities levels are within the 0.9–1.7% range, as they were for Lot 788435, the claim limitation is met. (*See* Kirsch Tr. 820:20–821:15.)

[4] For impurities levels in Lot 310571 that were below the claimed range at the initial time-point but above it at 3 months, the levels necessarily passed through the claimed range during that time period. (FF¶¶117–21.)

Inc., 182 F.3d 1315, 1319 (Fed. Cir. 1999). There also is no dispute a POSA could have measured those properties using routine techniques. (FF¶74.) Par's internal documents thus evidence inherent properties of Original Vasostrict as sold and used.

pH limitation (both Asserted Patents): The only limitation not expressly met by Original Vasostrict when it had the claimed impurities is pH. However, because Original Vasostrict's pH abutted the claimed pH, that difference is presumed obvious. *See Woodruff*, 919 F.2d at 1577 (presumption applied because "*more than 5%* to about 25%" abuts "about 1–*5%*"); *In re Brandt*, 886 F.3d 1171, 1174, 1177–78 (Fed. Cir. 2018) (presumption applied because "*less than 6* pounds per cubic foot" abuts "between *6* and 25 pounds per cubic foot"). Here, the asserted claims recite "a pH of 3.7–3.9." (FF¶¶58–59.) Par asserts that range encompasses pHs from 3.65 to 3.94, with rounding. (FF¶62.) The Original Vasostrict label taught "pH 3.4–3.6," up to 3.64 with rounding. (FF¶¶88, 156.) Lot 788435 met the claimed impurity levels with an abutting pH of 3.6. (FF¶91.)[5] The claimed pH 3.65 lower boundary abuts the Original Vasostrict's pH 3.64 upper boundary. (FF¶¶154.)

Moreover, Par's expert Dr. Kirsch admitted a POSA would have expected at

[5] Notably, commercial Lot 788436 had a pH in the claimed range (3.7) on release, while registration Lot 310571 had a pH within the claimed range (3.8) during its shelf life. (FF¶¶116, 126.) These forays into the claimed range were permitted by the FDA-approved specifications for Original Vasostrict, which allowed a release pH of 3.3–4.0, and a shelf life pH of 2.5–4.5. (FF¶¶89–90.)

least part of the claimed pH range to yield the same properties as the prior art range. (FF¶¶158, 166, 203, 206); *In re Peterson*, 315 F.3d at 1329 (presumption applies if abutting ranges expected to have same properties). Notably, the Asserted Patents describe Original Vasostrict's pH as "about 3.4 to ***about***[6] 3.6," which Dr. Kirsch agreed could include pHs above 3.64, overlapping the claimed range. (FF¶¶62, 79); *In re Patel*, 566 Fed. App'x. 1005, 1010 (Fed. Cir. 2014) (presumption applies "where there is a teaching in the prior art that the end points of the prior art range are approximate, or can be flexibly applied.").

Because the only difference between the prior art and the claimed invention is the abutting pH values, the presumption of obviousness applies.[7]

B. Par Cannot Rebut The Presumption Of Obviousness

Because the presumption applies, Par needed to proffer evidence "that the claimed range is critical, generally by showing that the claimed range achieves unexpected results relative to the prior art range," or that "the prior art teaches away from the claimed invention." *Peterson*, 315 F.3d at 1330 (internal marks omitted); *In re Geisler*, 116 F.3d 1465, 1471 (Fed. Cir. 1997). Although the ultimate burden

[6] All emphasis is added.

[7] In *Tris Pharma, Inc. v. Actavis Lab'ys FL, Inc.*, in contrast, this Court declined to apply the presumption because the overlapping efficacy times were ***not*** the only difference between the asserted claims and the prior art. 503 F. Supp. 3d 183, 203 (D. Del. 2020).

of persuasion never leaves Defendants, because Par failed to meet its burden of production, the presumption alone is sufficient to carry Defendants' burden. *See Genentech*, 946 F.3d at 1341; *E.I. DuPont de Nemours & Co. v. Synvina C.V.*, 904 F.3d 996, 1006 (Fed. Cir. 2018).

Viewed either way, Par's proffer fails for several reasons.

1. Par's criticality evidence is not commensurate in scope

Par's criticality evidence is insufficient because it is not "***commensurate in scope with the claimed [pH] range***." *Peterson*, 315 F.3d at 1330. In *Peterson*, the patentee proffered evidence of unexpected properties of an alloy comprising 2% rhenium to support criticality of the claimed range "about 1–3% rhenium." *Id*. at 1328. The Federal Circuit held it did "not evidence unexpected results for the entire claimed range of about 1–3% rhenium." *Id*. at 1331.

The same is true here. *First*, Dr. Kirsch conceded any difference in stability between pH 3.64 (outside the claimed range) and 3.65 (inside the claimed range) would "be so small that you wouldn't be able to detect it." (FF¶¶203, 215.) Thus, Par cannot show the full pH range 3.7–3.9 is critical compared to values outside that range.

Second, Par's evidence concerns formulations ***manufactured*** in the claimed pH range 3.7–3.9, *i.e.*, they have that pH initially. (FF ¶¶168–71, 182, 194–95, 214.) But Par alleges the Asserted Patents cover formulations ***manufactured <u>outside</u>*** the

claimed range, that may ***drift into*** the claimed range during their shelf lives, even for a few minutes. (FF¶61.) Yet neither Dr. Kirsch, nor the named inventors, could identify ***any*** evidence comparing stability of formulations that drifted into the claimed pH range after manufacture with those that remained outside the claimed range. (FF¶¶168–71, 182, 195, 214.) Par's evidence thus is not "commensurate in scope" for this additional reason.

Third, Par's criticality evidence concerns particular vasopressin formulations with an acetate buffer and no chlorobutanol, (FF¶¶172, 183, 192), but the claims broadly cover ***all*** formulations meeting the pH and impurities limitations. (FF¶¶58–59, 198.) This is particularly problematic regarding inclusion of a buffer. Inventor Kannan told the PTO that buffer choice has an "unpredictable" effect on impurity levels over a formulation's shelf life. (FF¶196.) And inventor Kenney testified that stability testing of a formulation with a particular buffer and without chlorobutanol cannot be generalized across all claimed formulations. (FF¶¶197, 223.)

Par's "criticality" evidence thus cannot rebut the presumption of obviousness as a matter of law.

2. Par's evidence does not otherwise show criticality

Even considering the merits, Par's proffered evidence does not show criticality because formulations with pHs in the claimed range have only minimal, unsurprising differences, if any, compared to those outside. But alleged unexpected

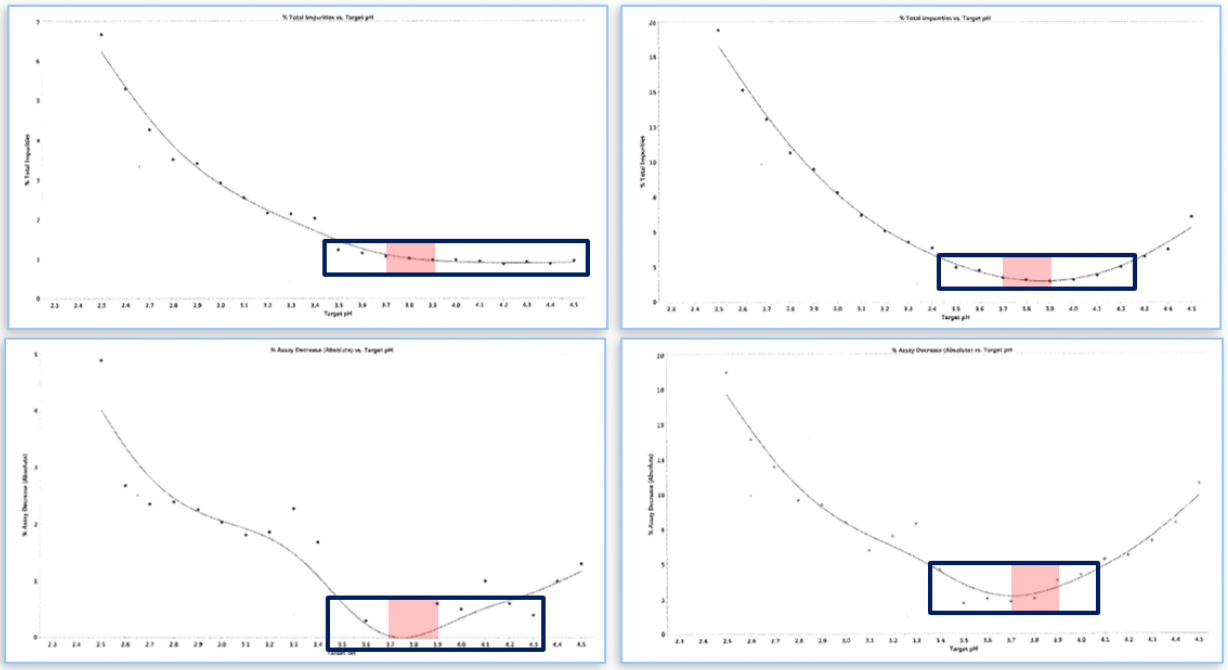
results must be "different in kind and not merely in degree from the results of the prior art." *Galderma Lab'ys, L.P. v. Tolmar, Inc.*, 737 F.3d 731, 739 (Fed. Cir. 2013) (internal marks omitted). "Results which differ by percentages are differences in degree rather than kind, where the modification of the percentage is within the capabilities of one skilled in the art at the time." *Id*. (comparable tolerability of 0.1% and 0.3% does not support non-obviousness). For example, in *In re Aller*, the court found that a 9–25% increase in product yield was insufficient for non-obviousness. 220 F.2d 454, 457 (C.C.P.A. 1955).

Par's evidence does not show a difference in kind and is similarly insufficient.

a. Par's pH studies do not show criticality

Par submitted pH stability data to allege criticality during prosecution of the patent family, and later incorporated the data into Examples 9 and 10 of the Asserted Patents. (FF¶¶189–90.) The data included plots of the impurity levels and remaining vasopressin (assay) as a function of pH within the range 2.5–4.5, after storage for four weeks at both 25°C and 40°C. (FF¶¶188, 200, 281.)

These data do not show criticality. Defendants' analytical stability expert Dr. Chyall testified that "when you look at the data as a whole," there is broad range of pH values with comparable stability and "no showing of criticality." (Chyall Tr. 591:2–7; FF¶201.) Dr. Chyall's annotation of the submitted plots plainly shows—at best for Par—slight differences in degree:



(DDX4-15–18 (Dr. Chyall's annotated demonstratives of DTX-10.2362–65); FF¶201.). As Dr. Chyall explained, the regions of comparable stability (blue boxes) extend beyond the claimed range (pink highlight). (FF¶201.) The differences in impurities and assay between pHs inside and outside the claimed range are at most a few tenths of a percent. (FF¶¶201–02.) Also, some pH values outside the claimed range had ***lower*** impurities or ***higher*** assay than some within the range, negating criticality. "If [the patentees] want to claim a range, they need to show unexpected results for the ***entire*** claimed range." *Patel*, 566 F. App'x at 1012.

To argue criticality at trial, Dr. Kirsch focused only on the 40° C data, testifying it showed a "statistically significant" difference in stability across the claimed pH range. (Kirsch Tr. 783:21–786:22.) But "statistical significance" is not "criticality." Dr. Kirsch acknowledged that statistical significance merely indicates

whether a measured difference is "a real difference" as opposed to "one that maybe is attributable to random error in the measurement process." (FF¶204.) But even a "real" difference, if only in degree, does not establish criticality. Indeed, in *Aller*, the Federal Circuit found a minor improvement in yield, although real, did ***not*** support non-obviousness. *See Aller*, 220 F.2d at 457. No case holds that statistical significance establishes criticality.

But it can foreclose it. While Dr. Kirsch alleged statistically significant differences in stability between pH 3.7–3.9 and ***some pH values*** outside the range, he conceded his own analysis showed there was ***no*** statistically significant difference in stability between the claimed pH range and pH 4.0, outside the claimed range. (FF¶206.) That admission is fatal, as it means Par cannot "show unexpected results for the ***entire*** claimed range," as required for criticality. *Patel*, 566 F. App'x at 1012.[8]

Dr. Kirsch's "answer" to this problem was that differences in ***kind*** are "not relevant to drug stability processes." (Kirsch Tr. 803:8–19.) But there is no special criticality rule for "drug stability processes." Dr. Kirsch cannot rewrite the law.

[8] A statistical analysis conducted by respected biostatistics expert Dr. Marais, who Dr. Kirsch selectively relied upon, showed ***no*** statistically significant difference for the claimed pH range compared to many other pH values as well. (FF¶¶207–10.)

b. Reformulated Vasostrict comparisons do not show criticality

Par's attempt to show criticality by comparing Reformulated Vasostrict to Original Vasostrict and Eagle's ANDA product, (FF¶172), also fails.

First, the comparisons do not show any stability difference is attributable to pH because the products have different formulations. (FF¶¶184, 186.) Reformulated Vasostrict includes acetate buffer and omits chlorobutanol, while Original Vasostrict and Eagle's product include acetic acid and chlorobutanol, among other differences. (FF¶183.) Though Dr. Kirsch suggested these formulation differences do not matter, (Kirsch Tr. 802:3–21), inventor Kenney contradicted him, explaining that he "wouldn't be comfortable" extrapolating studies showing Reformulated Vasostrict is most stable at initial pH 3.8 to other formulations, "based on the non-controlled variables." (FF¶186.)

Second, the comparisons do not show the claimed pH provides ***any*** practical stability benefit. Both Reformulated and Original Vasostrict have the same shelf life and impurities specifications. (FF¶185.) Par's clinical expert Dr. Coralic was not even aware Vasostrict had been reformulated before this case. (FF¶¶180, 185). And while Par's witnesses suggested it has data supporting a longer shelf life for Reformulated Vasostrict, (FF¶185), no such data was presented at trial, *id.*, and there is no evidence Par submitted such data to the FDA. *Id.*

Lastly, the numerical impurity differences between Reformulated Vasostrict and batches of Original Vasostrict and Eagle's ANDA Product at end of shelf life were about 1–2%. (FF¶177.) Such minor differences in degree cannot establish criticality. *See Galderma*, 737 F.3d at 739; *Aller*, 220 F.2d at 457. Indeed, the end-of-shelf-life total impurity percentages for all three products were between 3.5–5.5%, well below the FDA-approved 17% requirement. (FF¶175.)

3. Par's evidence does not show teaching away

Par's proffered references do not teach away from the claimed pH. A reference teaches away only "when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant." *Gator Tail, LLC. v. Mud Buddy, LLC*, 618 F. App'x 992, 998–99 (Fed. Cir. 2015) (internal marks omitted). But "[a] known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use." *In re Gurley*, 27 F.3d 551, 553 (Fed. Cir. 1994).

Par's teaching away evidence fails for several reasons. *First*, like criticality, "[e]vidence concerning whether the prior art teaches away from a given invention must relate to and be ***commensurate in scope*** with the ultimate claims at issue." *Idemitsu Kosan Co. v. SFC Co.*, 870 F.3d 1376, 1381 (Fed. Cir. 2017). But neither Par nor any of its witnesses could identify any teaching evaluating stability of

vasopressin formulations whose pH drifted into the claimed range after manufacture. (FF¶212.) Bi and the Biopharmaceutical and Chemistry Reviews of Original Vasostrict address only formulations ***manufactured*** at a particular pH. (FF¶¶220, 224.) Thus, this case is like *MeadWestVaco Corp. v. Rexam Beauty & Closures, Inc.*, where the Federal Circuit held an article discouraging "fragrance-specific uses" of a product did not teach away from broader claims covering general-purpose uses, because the evidence was not commensurate with the claim scope. 731 F.3d 1258, 1264 (Fed. Cir. 2013).

Second, prior art vasopressin formulations were available at the claimed pH, thus undermining Par's contention that POSAs would be taught away from the claimed range. *See Hoffmann-La Roche Inc. v. Apotex Inc.*, 748 F.3d 1326, 1331 (Fed. Cir. 2014) (finding one article's "contrary findings substantially undermined th[e] interpretation" provided in another article offered for teaching away). Prior art Pitressin was sold with pHs in the claimed range on release and during shelf life. (FF¶216.) Lithuanian Patent No. 4487 explicitly taught using a pH within the claimed range. *Id.* While Dr. Kirsch sought to discredit that reference because it related to animal-derived vasopressin, (FF¶217), he presented no evidence that pH impacts synthetic and animal-derived vasopressin in different ways. (FF¶¶217–19.)

Third, Bi studied only formulations with phosphate buffers. (FF¶223.) The asserted claims, in contrast, permit use of any buffer, or no buffer at all. As inventor

Kenney conceded, one cannot generalize pH study results "regardless of the type of buffers or components used in vasopressin formulations" "unless we studied all buffers." *Id.* Thus, Bi cannot teach away from a pH of 3.7–3.9 for all formulations.

Lastly, the statements in FDA's Biopharmaceutics and Chemistry Reviews of Original Vasostrict that a pH of 3.4–3.6 is "critical" because vasopressin degradation "accelerates" at pHs outside that range do not teach away. (FF¶¶220–22.) Foremost, Dr. Kirsch conceded these statements do not teach away from manufacturing a formulation at 3.4–3.6, and allowing it to drift into the claimed range for as little as a few minutes. (FF¶214.) Indeed, the FDA simultaneously approved pH specifications for Original Vasostrict—the product in the Reviews—permitting it to drift between pH 2.5–4.5 over its shelf life. (FF¶221.) Further, the mere knowledge of drawbacks does not render a claimed invention non-obvious; benefits and drawbacks of a claimed invention must be weighed accordingly. *See Hoffman-La Roche Inc. v. Apotex Inc.*, 748 F.3d 1326, 1333 (Fed. Cir. 2014) ("A higher frequency of diarrhea does not necessarily teach away …. modest gastrointestinal side effects must be weighed in light of the benefits of the drug."). The FDA review provided no data showing the extent of any "accelerat[ion]" of degradation around 3.4–3.6, (FF¶222), and so could not teach away from the full claimed range.

Accordingly, Par's "teaching away" arguments also fail, and Par has failed to rebut the presumption of obviousness. The asserted claims should be found obvious.

C. Obviousness Under Traditional Framework

Even under a traditional obviousness analysis, the asserted claims would be obvious. Clear and convincing evidence shows that a POSA making a vasopressin formulation at the priority date would be motivated to adopt Original Vasostrict's formulation and refrigerate it to minimize impurities, as its label instructed. (FF¶¶75–76, 125, 162, 185.) According to its specifications, Original Vasostrict was permitted to drift into the claimed pH range, meeting the claims according to Par's interpretation for infringement, and indeed did so. (FF¶¶161, 163.) Par has not come forward with any secondary considerations showing the nonobviousness of a formulation that does so. (*See* Section II.B, *supra*.)

III. THE ASSERTED PATENTS ARE UNENFORCEABLE

The Asserted Patents are unenforceable due to repeated acts of inequitable conduct committed during prosecution of the patent family, which taint the Asserted Patents. A patent is unenforceable where "the patent applicant (1) misrepresented or omitted information material to patentability, and (2) did so with specific intent to mislead or deceive" the PTO. *Intellect Wireless, Inc. v. HTC Corp.*, 732 F.3d 1339, 1341–42 (Fed. Cir. 2013). "[I]nequitable conduct infects the invention itself, and all claims which form a part of that invention." *Robocast, Inc. v. Microsoft Corp.*, 21 F. Supp. 3d 320, 338 (D. Del. 2014). Thus, "the taint of a finding of inequitable conduct can spread from a single patent to render unenforceable other related patents and

applications in the same technology family." *Therasense, Inc. v. Becton, Dickinson and Co.*, 649 F.3d 1276, 1288 (Fed. Cir. 2011). As explained below, inventor Kannan submitted two false declarations during prosecution of the parent '239 Patent, and a third during prosecution of another related patent, the '478 Patent, which tainted prosecution of the Asserted Patents.

A. Kannan Submitted Three False Declarations That Were Material

Kannan's three false declarations were material to prosecution. "[A]s a general matter, the materiality required to establish inequitable conduct is but-for materiality," that is, a showing the Examiner would not have allowed the claims "but for" the alleged inequitable conduct. *See Therasense*, 649 F.3d at 1291. However, the Federal Circuit "recognize[s] an exception in cases of egregious misconduct": "[w]hen the patentee has engaged in affirmative acts of egregious misconduct, ***such as the filing of an unmistakably false affidavit***, the misconduct ***is material***." *Id.* at 1292 (citations omitted); *see also, e.g.*, *Rohm & Haas Co. v. Crystal Chem. Co.*, 722 F.2d 1556, 1571 (Fed. Cir. 1983) ("[T]here is no room to argue that submission of false affidavits is not material."). That is the case here.

1. Kannan's False Inventorship Declaration

During prosecution of the parent '239 Patent, the Examiner rejected the pending claims over the April 2014 Original Vasostrict Label ("2014 Label"), relying on its disclosure of clinical, formulation, dosing, pH and refrigerated storage

information. (FF¶¶245–47.) In response, Kannan and Kenesky represented the inventors invented ***all*** the subject matter of the 2014 Label, in order to disqualify it as prior art.[9] (FF¶¶248–59.) The Examiner then disqualified the 2014 Label as a direct result of Kannan's declaration: "[t]he declaration by Inventor Vanayagam [*sic*] Kannan includes an unequivocal statement that he and Matthew Kenney invented the subject matter disclosed in the FDA Label and relied upon in the rejection (¶6–7). …" (FF¶260.)

Kannan's declaration was false. (*See* FF¶¶258, 261–65.) Kannan admitted his only contribution to the 2014 Label was evaluating data on refrigeration of diluted vasopressin, and not all the subject matter as he and Kenesky represented. (FF¶263.) The other inventor referenced in the declaration, Kenney, could not recall making ***any*** contribution to the 2014 Label. (FF¶262.) Kannan and Kenesky's submission of an unmistakably false declaration was material to prosecution of the '239 patent as a matter of law.[10] *Therasense*, 649 F.3d at 1291; *Rohm & Haas*, 722 F.2d at 1571.

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[9] Under the AIA, an applicant can disqualify a reference as prior art if it is a "disclosure made 1 year or less before the effective filing date … [that came] directly or indirectly from ***the inventor or a joint inventor***." 35 U.S.C. § 102(b)(1)(A).

[10] Clear and convincing evidence also shows that it was but-for material, as the 2014 Label disclosed or rendered obvious every limitation of the ultimately issued '239 patent claims. (FF¶¶273–75.) Notably, those issued claims include ***no refrigeration limitation***. (FF¶¶271–72.)

This case is strikingly similar to *Intellect Wireless.* There, an inventor submitted a declaration to disqualify prior art, falsely averring that "the claimed invention was actually reduced to practice and was demonstrated at a meeting" before publication of the prior art. 732 F.3d 1339, 1342. The Federal Circuit affirmed that the false statements themselves established materiality, stating "[i]t is undisputed that [the inventor's] original declaration was unmistakably false. ***Absent curing, this alone establishes materiality***." *Id*. Similarly here, Kannan and Kenesky overcame the 2014 Label by averring the inventors invented the subject matter therein. Like in *Intellect Wireless,* the statement was not true and ***never*** cured. (FF¶¶267–268.)

None of Par's arguments can excuse it from the consequences of its conduct. Par contends the false statements were not material, either because they did not impact prosecution, or because they are cumulative of other information the Examiner must have known. But egregious affirmative misconduct through false statements are material by law. *Therasense*, 649 F.3d at 1291; *Rohm & Haas*, 722 F.2d at 1571; *Refac Int'l, Ltd. v. Lotus Dev. Corp.*, 81 F.3d 1576, 1583 (Fed. Cir. 1996). Thus, these arguments are irrelevant.

Par's arguments also defy common sense.

First, Par will argue the Examiner could not have understood Kannan's declaration to mean he and Kenney invented ***all*** the relied-upon subject matter of the

2014 Label, since she would have known vasopressin had been used for decades. (Cross Tr. 514:14–23.) In essence, Par suggests that Kannan and Kenesky's false submission should be excused because it was ***so false*** it should not have been believed. That type of argument is why the Federal Circuit has repeatedly said "there is no room to argue that submission of false affidavits is not material." *Rohm & Haas*, 722 F.2d at 1571. And accepting *arguendo* the Examiner "should have known" it to be false, Kenesky—with access to the inventors—would even more certainly have known of its falsity.

Whatever Par says now, it is also clear that the Examiner ***did*** accept the declaration as true. The Examiner asked for an "unequivocal statement" that the inventors invented "all" of the subject matter she relied upon "if possible," and upon receiving it, accepted it and withdrew the rejection. (FF ¶¶254, 259–260.)

Second, Kannan's testimony that he only intended to suggest he contributed to refrigerated storage as part of the ***combination*** of subject matter in the 2014 Label is a *post hoc* justification that is contrary to the plain language of the declaration and the context of prosecution. After the Examiner's rejection over the 2014 Label, Kenesky submitted a *draft* declaration to the Examiner, aimed at disqualifying it as prior art, but that draft ***did not mention refrigerated storage***. (FF¶¶252–53.) During a subsequent interview, the Examiner recommended amending the draft to provide "an ***unequivocal statement*** that one or more joint inventors invented ***all of the***

subject matter relied upon, if possible." (FF¶254.) Kenesky responded that Kannan "would be able to make this statement," knowing that it would be relied upon to disqualify the FDA reference. (FF¶¶255, 268.) Just days later, Kenesky submitted the revised, signed declaration that Kannan and Kenney "invented the subject matter of the 2014 Label that is cited in the Office Action," and that "[t]he FDA obtained this information from me and Matthew Kenney, ***as we invented this subject matter***." (FF¶¶255–258.) Kenesky and Kannan confirmed they never told the Examiner the inventors contributed only to refrigerated storage. (FF¶¶267–68.) The declaration's plain language and Examiner discourse leaves no room for Kannan's explanation.

Finally, Par may argue that the 2014 Label was not material because it did not explicitly teach the '239 Patent's degradation limitation. But the Examiner had already found similar levels of the same degradants to be inherent in the claimed formulations. (FF¶274.) And by the time the 2014 Label was disqualified, Par's own internal data showed that Original Vasostrict described in the 2014 Label met the limitation. (FF¶275.)

Clear and convincing evidence thus shows that Kannan's inventorship declaration was material as a matter of law and in fact.

2. Kannan's False Normalization Declarations

During prosecution of the '239 and '478 Patents, Kannan submitted two more false declarations to convince the Examiner the claimed pH ranges were ***critical*** to

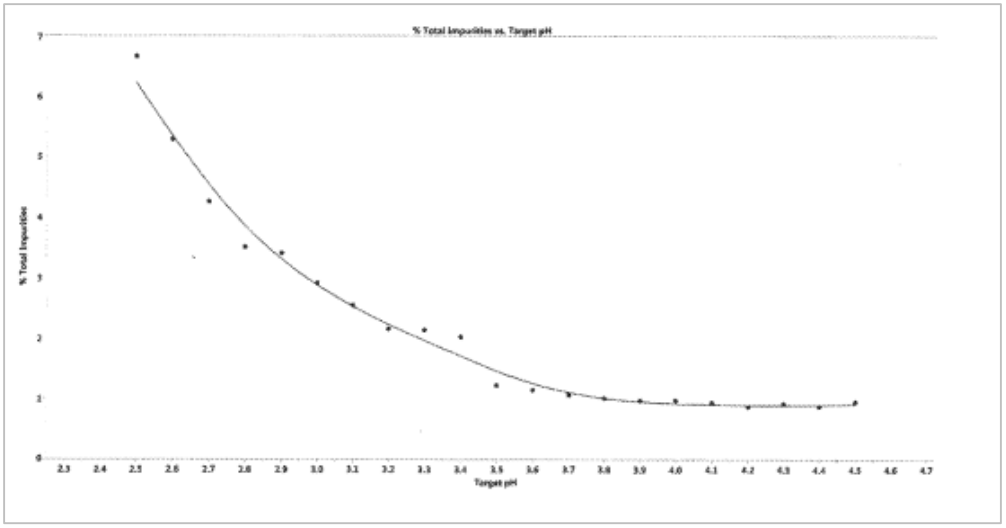
stability and inventive over the prior art. In the ’478 Patent prosecution, the Examiner rejected the claims over the label for a vasopressin product sold by Pharmaceutical Partners of Canada (“PPC”), which taught a formulation with pH range 2.5–4.5. (FF¶¶279–280.) During the ’239 Patent prosecution, after disqualification of the 2014 Label, the Examiner rejected the claims over PPC as well. (FF¶297.)

To overcome these rejections, Par argued that the pH limitations were ***critical*** to stability, and submitted data from the same pH studies that Par uses to allege criticality here. (FF¶¶279–284). The applicants presented the data from two separate studies, conducted months apart, together in the same graphs. (FF¶¶281–284, 297–298.) The first study addressed the top end of the PPC pH range (3.5–4.5), and the second addressed the bottom end (2.5–3.4). (FF¶¶283–284). While the same lot of vasopressin was used in both studies, it had degraded in the intervening eight months such that the formulations used in the second study had significantly higher starting impurity levels than those used in the first study, which included the claimed pH range. (FF¶¶282–284). Thus, the claimed pH range ***started the experiment*** with fewer impurities than pH 2.5-3.4. (FF¶¶303–304).

When reporting the results to the Examiner, the inventors accounted for differences in the starting ***assay*** values by ***normalizing*** the data, thus showing only the ***change*** over four weeks. (FF¶¶285–287, 300). But they did not do that for

impurities. (FF¶¶285–287.) Instead, they reported only the total impurities present at the end of the study, even though the starting impurity levels were different for different pH values. (FF¶¶282–286, 300.)

The Examiner actually noticed a "break in the data" for both assay and impurities between pH 3.4 and 3.5, the precise spot where data from the two studies was combined, an example of which can be seen in the figure below submitted to the Examiner. (FF¶289–291.)



(DTX-7.1885.) The Examiner hypothesized that the break "may possibly be attributed to differences between the two experimental batches" (FF¶289), and sought an explanation. (FF¶¶289–291). She reiterated her concern during an interview. (FF¶290.)

In response, Kannan submitted a declaration in the '478 Patent prosecution stating that the applicants had normalized ***both*** the impurities and assay data, that "because pH was the only variable that was not normalized, … [the] % total

impurities results for each formulation were attributable to changes in pH," and that he was "not aware of any other factors that would account for the differences in the results for each formulation." (FF¶¶292–295.) Upon receipt of Kannan's declaration, the Examiner allowed the claims. (FF¶296.)

Subsequently, when the Examiner rejected the '239 Patent claims over PPC, Kannan submitted an almost identical declaration. (FF¶¶297–298.) The Examiner allowed the '239 Patent claims as well, stating that "[t]he [Kannan] declaration under 37 CFR 1.132 filed May 22, 2017 is sufficient to overcome an obviousness rejection over Pharmaceutical Partners of Canada because it establishes the criticality of the claimed pH range of 3.5 to 4.1." (FF¶299.)

Kannan's normalization declarations were unmistakably false. At trial, Kannan admitted that the impurities data had ***not*** been normalized, and the "difference in the starting point of impurities" could possibly explain the "break" in the data, as the Examiner suspected. (FF¶¶300, 304–05.) Further, Kannan ***knew*** his representation was false, because he had received normalized impurities data just nine days earlier. (FF¶301.) He considered sending them to Par's legal counsel, but they ultimately were not submitted to the Examiner. (FF¶301.). As Dr. Chyall explained, had they been submitted, at least the normalized impurities data at 25° C would have told a very different story about the impact of pH 3.7-3.9 on impurity levels than the non-normalized data—namely, that it was not critical. (FF¶308.)

Because Kannan falsely represented the data was normalized, Kannan's misconduct is material to prosecution of the '239 and '478 Patents as a matter of law. *Therasense*, 649 F.3d at 1291; *Rohm & Haas*, 722 F.2d at 1571. But clear and convincing evidence also shows that it was independently but-for material, as it caused the Examiner to disregard her legitimate concerns about whether the impurities profile was due to data having been obtained in two separate studies, rather than the impact of pH. (FF¶289–291.) That in turn was her basis for allowing the claims of both patents. (FF¶¶295–299.)

Rohm & Haas is instructive. There, in response to the Examiner's rejection of claims to a herbicide, the applicants submitted test data via affidavits purporting to show advantageous properties of the claimed invention compared to prior art. 722 F.2d at 1561–62. But the affiants omitted that the claimed invention and the prior art were tested under different experimental conditions. *Id.* Although the patentee argued that it eventually provided all of the data, the Federal Circuit found the misrepresentations and omissions to be material. *Id*. at 1565–66, 1570–71.

None of Par's proffered explanations are persuasive. *First*, Kannan claimed it was "not necessary" to normalize impurities. (Kannan Tr. 722:24–723:9.) But as Dr. Chyall showed, and Kannan conceded, the starting ***impurities*** levels between the two studies also were significantly different, and the reason for the break in the data, warranting normalization. (FF¶¶303–305, 308.)

Second, Kannan said that, when he ***stated*** "pH was the only variable not normalized," (Kannan Tr. 724:17–25:1), he ***meant*** only that "pH was not the constant between formulations." (*Id.* 726:2–11.) To the extent it can be understood, this explanation is belied by the express statements in the declaration. Kannan defined "normalization" and explained its use in combining data from multiple studies just one paragraph earlier. (FF¶¶294, 298.) Kannan's assertion he defined "normalization" in one paragraph, used that definition for assay data, but did not intend it to apply to impurities data just one paragraph later, is simply not credible.

Finally, like the patentee in *Rohm & Hass*, Par has suggested that the Examiner could have generated the normalized charts herself. (FF¶306.) The Court should reject this argument because "[i]t does not suffice that one knowing of misrepresentations in an application or its prosecution merely supplies the examiner with accurate facts without calling his attention to the untrue or misleading assertions sought to be overcome, leaving him to formulate his own conclusion." *Intellect Wireless* at 1343 (quoting *Rohm & Haas*, 722 F.2d at 1572). The fact is the Examiner accepted that all data ***was*** normalized. (FF¶306.) Cases like *Intellect Wireless* and *Rohm & Haas* preclude Par's argument that the Examiner should have realized Kannan's representations were false, found, normalized and plotted the data, and figured out the truth for herself.

Clear and convincing evidence thus shows Kannan's normalization declarations also were material as a matter of law and fact.

B. The Single Most Reasonable Inference Is Intent To Deceive

Clear and convincing evidence also shows that the single most reasonable inference is that Kannan and Kenesky submitted the false declarations with intent to deceive. To find inequitable conduct, "the specific intent to deceive must be the single most reasonable inference able to be drawn from the evidence" that is available. *Aventis Pharma S.A. v. Hospira, Inc.*, 675 F.3d 1324, 1335 (Fed. Cir. 2012) (internal marks omitted). However, "[d]irect evidence of intent or proof of deliberate scheming is rarely available in instances of inequitable conduct, but intent may be inferred from the surrounding circumstances." *Critikon, Inc. v. Becton Dickinson Vascular Access, Inc.*, 120 F.3d 1253, 1256 (Fed. Cir. 1997). For this reason, "in the absence of a credible explanation, intent to deceive is generally inferred from the facts and circumstances surrounding a knowing failure to disclose material information." *Bruno Indep. Living Aids, Inc. v. Acorn Mobility Servs. Ltd.*, 394 F.3d 1348, 1354 (Fed. Cir. 2005).

In the context of false declarations, like here, to focus on the inventor's "actual state of mind" is "legal error." *Rohm & Haas*, 722 F.2d at 1571. Rather, "[t]he inference [of intent to mislead] arises not simply from the materiality of the affidavits, but from the affirmative acts of submitting them, their misleading

character, and the inability of the examiner to investigate the facts." *Paragon Podiatry Lab., Inc. v. KLM Lab., Inc.*, 984 F.2d, at 1191 (Fed. Cir. 1993).

Par offered no credible explanation for the false declarations, and thus intent to deceive is the single most reasonable inference. Kannan admitted that he knew they were intended to convince the Examiner to withdraw her rejections when he made them. (FF¶¶269, 302.) It is further clear that both Kannan and Kenesky understood the Examiner required an "***unequivocal statement***" from the '239 Patent inventors that they invented "***all of the subject matter***" in the 2014 Label to disqualify it. (*See* FF¶¶254–59, 269.) Kannan's explanation that he intended only to declare the inventors invented the ***combination*** of subject matter in the 2014 Label based on his purported contributions to refrigerated storage is not credible. Kenesky offered no explanation for his conduct.[11]

Likewise, Kannan knew the Examiner would rely on his normalization declarations to explain the break in the data, given her expressed concern over using data from two different studies conducted at different times. (FF¶¶289–95, 302.) Kannan's proffered explanation for the false statements—that he intended the term

[11] Par asserted privilege over Kenesky's knowledge and intent regarding the inventorship declaration (Tr. 672:7–673:4; D.I. 278-2). *See Ansell Healthcare Prod. LLC v. Reckitt Benckiser LLC*, No. 15-CV-915-RGA, 2017 WL 6328149, at *4 (D. Del. Dec. 11, 2017) ("[P]rivilege cannot be used both as a sword and a shield.").

"normalization" to mean different things in successive paragraphs of his declarations, (Kannan Tr. 724:17–726:22)—also was not credible. Par's effort—as to the 2014 Label and normalization declarations—to blame the Examiner for not herself figuring out their deceit only reinforces their intent.

Because there is no "credible explanation" for Kannan's false declarations and clear and convincing evidence shows intent to deceive is the single most reasonable inference, the Court should find Kannan and Kenesky committed inequitable conduct during prosecution of the '239 and '478 Patents. *See Bruno Indep. Living Aids*, 394 F.3d at 1354.

C. The Inequitable Conduct Infected The Asserted Patents

As noted, "inequitable conduct infects the invention itself, and ***all claims*** which form a part of that invention." *Robocast*, 21 F. Supp. 3d at 338. Thus, "the taint of a finding of inequitable conduct can spread from a single patent to render unenforceable other related patents and applications in the same technology family." *Therasense*, 649 F.3d at 1288. "Were this not the rule, a party committing inequitable conduct could avoid the consequences of that conduct through a scheme of divisional and continuation applications. The law does not countenance such a manipulation of the patent process." *Truth Hardware Corp. v. Ashland Prods., Inc.*, C.A. No. 02-1541-GMS, 2003 WL 22005839, at *1 (D. Del. Aug. 19, 2003). Infectious unenforceability exists here because the inequitable conduct during

prosecution of related patents had an "immediate and necessary relation" to the grant of the Asserted Patents. *See Consol. Aluminum*, 910 F.2d at 810–11.

First, the disqualification of the 2014 Label through the false inventorship declaration endured throughout prosecution of the Asserted Patents. After disqualification, the Examiner cited the 2014 Label only as an "evidentiary" reference, noting it did "***not need to be prior art***." (FF¶312.) As Drs. Cross and Park testified, had the 2014 Label not been disqualified, it would have rendered obvious the ultimately issued asserted claims. (FF¶¶313–14.) And as Dr. Chyall explained, because the 2014 Label describes an FDA-approved product with established shelf life stability and an optimized pH (which was lacking in the PPC reference), the four-week pH study conducted by the applicants would not even have addressed criticality over that formulation, much less established it sufficiently to secure allowance. (FF¶315.)

Second, the false normalization declarations also bear an "immediate and necessary relation" to the Asserted Patents because the applicants proffered the pH stability data and false declarations to establish criticality of the claimed pH over PPC during prosecution of the '239 and '478 Patents, then relied on the ***same data*** to establish criticality over the ***same*** reference during prosecution of the Asserted Patents. (FF¶¶317–18.) The Examiner already incorrectly believed the study data—

by then incorporated into Examples 9 and 10—showed criticality rather than the impact of stitching together the results of two studies. (*See id.*)

Clear and convincing evidence thus shows the false Kannan declarations tainted prosecution of the Asserted Patents, which should be held unenforceable.

IV. CONCLUSION

Defendants respectfully submit that the asserted claims should be held invalid for obviousness and unenforceable due to inequitable conduct. Amneal also respectfully requests that the Court exercise its discretion to decide invalidity and unenforceability even if it rules for Eagle on non-infringement, as it will moot further proceedings regarding Amneal's ANDA.

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Respectfully submitted,

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